Image AP/1651

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Attorney Docket Number: ETLI.P-002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Jaffe, Robert L.	Confirmation Number: 7877
Serial No.:	09/086,138	Group Art Unit: 1651
Filing Date:	May 28, 1998	Examiner: Gitomer, Ralph J.
For:	Determination of Cytotoxic Substances in Whole Effluent Samples	

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Signature

February 19, 2004
Date of Signature

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Jaffe	
Application No.: 09/086,138	Group Art Unit: 1651
Filed: 5/28/1998	Examiner: R. Gitomer
Title: Determination of Cytotoxic Substances in Whole Effluent Samples	Confirmation No.: 7877
Attorney Docket No.: ETLI.P-002	

BRIEF FOR APPELLANT

This brief is filed in support of Applicants' Appeal from the final rejection mailed 9/25/2003. Consideration of the application and reversal of the rejections are respectfully urged.

Real Party in Interest

The real party in interest is the inventor, Robert Jaffe.

Related Appeals and Interferences

This is the second appeal filed in this case. The previous Appeal was assigned Appeal No. 2002-0444 and was denied October 29, 2002, with a decision that presented a new ground for rejection.

I hereby certify that this paper and any attachments named herein are being deposited with the US Postal Service as first-class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on February 19, 2004.

Marina T. Larson

Marina T. Larson, PTO Reg. No. 32,038

February 19, 2004
Date of Signature

Status of Claims

Claims 1-15 are pending in this application and the subject of this appeal. No other claims have been presented.

Status of Amendments

All amendments presented in this case have been entered.

Summary of Invention

The present invention relates to a method for evaluating a liquid whole effluent sample for the presence of cytotoxic substances. As set forth in claim 1, the method comprises the steps of:

(a) obtaining a liquid whole effluent sample for testing, said sample being suspected of containing a plurality of potentially cytotoxic substances;

(b) combining a first aliquot of the liquid whole effluent sample directly with a culture of a particle-feeding flagellate said aliquot containing all of the potentially cytotoxic substances of the original sample obtained such that a measure of the toxicity of any combination of potentially cytotoxic substances can be obtained; and

(c) monitoring the growth rate of the particle-feeding flagellate culture in the presence of the aliquot of the liquid whole effluent sample, wherein a decrease in growth rate of the culture in the presence of the liquid whole effluent sample is indicative of the presence of cytotoxic agents in the liquid whole effluent sample. An exemplary particle-feeding flagellate is *Tetramitus rostratus* in its flagellate form.

Issues on Appeal

1. Are claims 1-15 in compliance with the written description requirement of 35 USC § 112, first paragraph?

2. Is the subject matter of claims 1 and 2 different from US Patent No. 5,387,508 such that the rejection under 35 USC § 102 should be reversed?

3. Is the subject matter of claims 3-15 unobviously different from US Patent No. 5,387,508 such that the rejection under 35 USC § 103 should be reversed?

Applicant submits that all of these questions should be answered in the affirmative, and that the rejections made by the Examiner should be reversed.

Grouping of Claims

With respect to the written description issue, all claims are argued as a single group, and stand or fall together.

With respect to the anticipation rejection, claims 1 and 2 are argued as a single group and stand or fall together.

With respect to the obviousness rejection the Examiner has failed to provide any reason to modify the teaching of the '508 patent to use *T rostratus* or other flagellates in a whole effluent toxicity test. Thus, the rejeciton of all of these claims should be reversed. In addition, the following claims have additional arguments as follows:

claims 3 and 6 are argued as a first group, and stand or fall together should the rejection of claim 1 be maintained;

claims 7-10 are argued as a second group that stands or falls together should the rejection of claim 1 be maintained;

claims 11-14 are argued as a third group that stands or falls together should the rejection of claims 1 and 7 be maintained; and

claim 15 is argued as a fourth group should the rejection of claim 1 be maintained.

Argument

In the Decision on the prior appeal, the Board observed that "the key to deciding the patentability issues in this case in our view is the interpretation and construction one places on the phrase 'whole effluent sample.' Applicant was encouraged to place limitations into the claims to further define this term, and this was done in an Amendment filed after the decision in accordance with 37 CFR § 1.196(b).

The Board of Appeal also noted that "it is unclear how the Examiner interprets this phrase," and directed that "any further rejection from the examiner should clearly state how the claims are being construed. Despite this direction, and the express request for the Applicant, the Examiner has still not stated what meaning he is giving to the term "whole effluent sample" and the reasons for such an interpretation. Indeed, in the Office Action mailed April 28, 2003, the Examiner simply reprinted portions of the previous action, and Appeal Brief, without regard for the fact that the claims had been changed.

There is evidence of record in this case, that the term "whole effluent toxicity" (WET" test, as defined by the United States Environmental Protection Agency (EPA) is the aggregate toxic effect of an effluent or receiving water measured directly with a toxicity test. (Declaration Under Rule 132 of Robert Jaffe, filed January 31, 2000) As further explained in the specification, the invention tests for "whole effluent toxicity, i.e., for toxicity of the combination of compounds, both organic and inorganic, which may be present in an effluent sample." (Page 4, lines 4-5).

1. Claims 1-15 are in Compliance with § 112

Claims 1-15 are rejected under 35 USC § 112, first paragraph, for lack off written description. This rejection is of the "new matter" type, because it is based on an amendment to the claim.

As amended, step (b) of claim 1 reads:

> (b) combining a first aliquot of the liquid whole effluent sample directly with a culture of a particle-feeding flagellate said aliquot containing all of the potentially cytotoxic substances of the original sample obtained such that a measure of the toxicity of any combination of potentially cytotoxic substances can be obtained;

The Examiner asserts that the phrase "measure of the toxicity of any combination of potentially cytotoxic substances can be obtained" is new matter, not supported by the original specification, and focuses particularly on the word "any". Applicant submit that this is semantics, and goes against the clear law on point which does not require there to be *in haec verba* supportfor an amendment to avoid new matter issues.

As stated in the specification, and as would be apparent to a person skilled in the art "whole effluent toxicity, i.e., for toxicity of the combination of compounds, both organic and inorganic, which may be present in an effluent sample." Taken individually, the chemical compounds may be toxic or non-toxic. A compounds may be present at such a low level that considered on its own it is non-toxic, but when present in the combination found in the whole effluent sample, there is a combined toxicity (wither additive or synergistic) observed. When the claim refers to "**any** combination of potentially cytotoxic substances" it is merely referring in different language to the "combination of compounds ... which **may** be present in an effluent sample." The tester does not know before testing if there are any toxic substances or combinations of substances in the sample. After testing, the presence or absence of toxicity is known, but the tester still does not know whether any observed toxicity is due to one or several components (although this can be addressed to some extent by the additional steps recited in dependent claims) or what these components are. The language of the claims, like the language of the specification reflect this by referring to "any combination" rather than "the combination" since it cannot be known if a combination even exists.

It is noted that in the Office Action dated September 25, 2003, the Examiner states that "the claim as written would appear to determine the toxicity of the sample only, not any combination of potentially toxic substances." These two are not separate things. The toxicity of a whole effluent sample is the toxicity of whatever combination (i.e., any combination) of potentially toxic substances are in the sample.

Thus, the claim scope is fully consistent with the invention as originally described. The rejection under 35 USC § 112, first paragraph, should be reversed.

2. Claims 1 and 2 are not anticipated by US Patent No. 5,387,508

Despite the specific instruction from the Board in its previous decision, the Examiner has still not provided his understanding of the scope of the claims. Instead, what he has argued is that the samples described in the cited reference do not expressly exclude whole effluent samples, and therefore that the present claims are anticipated. Applicants respectfully submit that the Examiner is misapplying the law as it relates to anticipation.

Whether or not a person skilled in the art would interpret liquid whole effluent samples as falling within the generic scope of the disclosure of the '508 patent (a fact that has not been established by the Examiner), the law is clear that disclosure of a genus does not *per se* anticipate a later claimed species.

Concepts of inherency may not be relied upon ti establish anticipation unless "the examiner [has provided] a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (BPAI 1990). Although the Examiner has not specifically asserted an "inherent disclosure" of the invention, the generalization and failure to focus on the specifics of the claimed invention and the reference, arguably amount to such an assertion. No arguments have been submitted to meet the *Levy* standard and show that statements that samples can be of different types, including gases and liquids, and may be processed or diluted, necessarily means that liquid whole effluent samples are disclosed in the '508 patent.

Furthermore, as observed in the MPEP, § 2131.03

> When the prior art discloses a range which touches, overlaps or is within the claimed range, but no specific examples falling within the claimed range are disclosed, a case by case determination must be made as to anticipation. In order to anticipate the claims, the claimed subject matter must be disclosed in the reference with "sufficient specificity to constitute an anticipation under the statute." What constitutes a "sufficient specificity" is fact dependent. If the claims are directed to a narrow range, the reference teaches a broad range, and there is evidence of unexpected results within the claimed narrow range, depending on the other facts of the case, it may be reasonable to conclude that the narrow range is not disclosed with sufficient specificity" to constitute an anticipation of the claims.

The genus of all toxicity tests is essentially a range, which encompasses tests that include whole effluent tests. Whole effluent tests are different from tests on concentrates or diluted samples of various types and different test systems are used in the art. Thus, the burden rests with the Examiner to show that from general tests the person skilled in the art would understand WET tests to be disclosed. This he has not done.

Finally, in this case, the Examiner has again asserted that Example 5, column 6 is a WET test. He has not explained under what meaning of the phrase "liquid whole effluent sample" this could be true. Applicant has stated in his 132 Declaration, ¶¶ 7 and 8, that neither of the experiments described in this example is a whole effluent sample. In the past, the Examiner has pointed to the fume portion of this example as a WET test. Fumes are not a liquid sample, however, and therefore even assuming that capture of a gas/vapor would not change the nature of the sample as a result of selective solubility in water, it is clearly not a liquid sample.

For these reasons, the rejection of claims 1 and 2 under 35 USC § 103 should be reversed.

3. Claims 3-15 Are Not Obvious over the '508 Patent

Each of claims 3-15 are rejected for obviousness. This rejection starts with the supposition that the anticipation rejection is correct. For this reason, the Examiner has provided no explanation as to why a person skilled in the art would find a suggestion of doing whole effluent tests in the '508 patent. Thus, the rejection of all of claims 3-15 should be reversed for this reason. Additional reasons also exist

The Organisms of Claims 3 and 6 are not suggested by the art

Claims 3 and 6 recite a list of organisms other than *T. rostratus*, for use as the particle-feeding flagellate of in the method of the invention. In support of this rejection, the Examiner states that using these flagellates in place of the one flagellate taught in the '508 patent would have been obvious because "one would have a high expectation of success in employing any known flagellate with the requisite qualities taught in the present specification." This argument suggests that the Examiner is improperly relying on the present specification in formulating his response. He has pointed to nothing in the '508 patent that suggests the use of other flagellates, or that defines the characteristics of such flagellates that would be desirable. The art relied upon, not the present specification, must be the basis for the rejection.

The Examiner continues with the observation that "the present specification teaches specific methods and examples only for T. rostratus." This is wholly irrelevant to the question of obviousness. 35 USC § 103 specifically provides that "patentability shall not be negatived by

the manner in which the invention was made." Thus, whether Applicant extended his invention through a flash of insight does not detract from its patentability, which can be only established based on the teaching of the art.

The additional method steps of claims 7-10 are not suggested by the art

Claim 7, and claims 8-10 dependent thereon, add additional step to the method of claim 1. In these steps, a second aliquot of the whole effluent sample is filtered through a filter having a defined pore size to produce a filtered whole effluent sample from which particulate materials greater in size than the defined pore size have been removed. This filtered whole effluent sample is combined with a second culture of particle-feeding flagellate and the growth rate of the particle-feeding flagellate culture in the presence of the filter whole effluent sample is determined. Comparing the growth rate of the particle-feeding flagellate culture in the presence of the filtered whole effluent sample to the growth rate in the presence of the unfiltered whole effluent sample allows a determination of whether the toxicity observed for the total sample is present as in the particulate part of the whole effluent sample, since the toxicity should go down if it is.

The Examiner's only explanation for the supposed obviousness of claim 7 is the statement made prior to the earlier appeal that the '508 patent teaches concentrating particulates in a column. It is assumed that this is still the only reason for this rejection.

As a first matter it is noted that the statement that the '508 patent "teaches concentrating particulates in column 7 Example 8" is utterly without support in the '508 patent. Example 8 deals with obtaining concentrates from urine of workers exposed to asbestos. The method used is an XAD2 column, which is one that concentrates organics (See Example 7). There is no mention of particulates in this example.

Furthermore, the Examiner's statement concerning the teaching of the '508 patent looks at claim 7 in isolation, and fails to take into account the limitations of the claim on which it depends. Claim 7 requires the performance of two tests, one on the whole effluent and one on the solution remaining after any particles are removed. There is no teaching of such a method in the '508 patent, and thus no suggestion of claim 7 and the claims dependent thereon.

The additional method steps of claims 11-14 are not suggested by the art

Claim 11, which is dependent on claim 7, adds an addition set of steps in which the toxicity of a particulate fraction is monitored. Thus, claim 11 calls for three separate assays. The third assay provides an important observation, since it provides information as to whether particulate and non-particulate toxicity are merely additive or whether they act synergistically to achieve a greater or lesser than additive toxicity in the whole effluent. This can be an important observation in determining the nature of the most effective form of remediation. Again, the examiner's only basis for the rejection is the faulty interpretation of Example 8 of the '508 patent. There is no suggestion of the invention of claims 11 and 14, and the rejeciton should therefvore be reversed.

The Method of Claim 15 Is Not Suggested

Claim 15 depends on claim 1, and recites the further step of monitoring the growth of a second culture of particle-feeding flagellate in the presence of the whole effluent and comparing the growth of the first and second cultures, wherein the mean size of the flagellates in the first and second cultures is different. The examiner has never stated where this limitation is suggested in the art, and there is no teaching of such a method in the '508 patent.

Conclusion

For the foregoing reasons, reversal of all of the rejections applied against the present application is urged.

Respectfully submitted,

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CLAIM ON APPEAL

1. A method for evaluating a whole effluent sample for the presence of cytotoxic substances comprising the steps of:

(a) obtaining a liquid whole effluent sample for testing, said sample being suspected of containing a plurality of potentially cytotoxic substances;

(b) combining a first aliquot of the liquid whole effluent sample directly with a culture of a particle-feeding flagellate said aliquot containing all of the potentially cytotoxic substances of the original sample obtained such that a measure of the toxicity of any combination of potentially cytotoxic substances can be obtained; and

(c) monitoring the growth rate of the particle-feeding flagellate culture in the presence of the aliquot of the liquid whole effluent sample, wherein a decrease in growth rate of the culture in the presence of the liquid whole effluent sample is indicative of the presence of cytotoxic agents in the liquid whole effluent sample.

2. The method of claim 1, wherein the particle-feeding flagellate is *Teramitus rostratus* in flagellate form.

3. The method of claim 1, wherein the particle-feeding flagellate is selected from the group consisting of *Chilodenella uncinata, Bodo caudataus, Cercomonas longicauda, Diplonema ambulator, Scytomonas pusilla* and *Bodo designis*.

4. The method according to claim 1, wherein a series of dilutions of the whole effluent sample is prepared and each dilution is individually combined with a culture of particle feeding flagellate to determine a dose response curve.

5. The method of claim 4, wherein the particle-feeding flagellate is *Teramitus rostratus* in flagellate form.

6. The method of claim 4, wherein the particle-feeding flagellate is selected from the group consisting of *Chilodenella uncinata, Bodo caudataus, Cercomonas longicauda, Diplonema ambulator, Scytomonas pusilla* and *Bodo designis*.

7. The method of claim 1, further comprising the steps of

filtering a second aliquot of the whole effluent sample through a filter having a defined pore size to produce a filtered whole effluent sample from which particulate materials greater in size than the defined pore size have been removed;

combining the filtered whole effluent sample with a second culture of particle-feeding flagellate;

determining the growth rate of the particle-feeding flagellate culture in the presence of the filter whole effluent sample; and

comparing the growth rate of the particle-feeding flagellate culture in the presence of the filtered whole effluent sample to the growth rate in the presence of the unfiltered whole

effluent sample, wherein as difference in the growth rate is indicative of the presence of particulate toxic substances in the whole effluent sample.

8. The method according to claim 7, wherein a series of dilutions of the filtered whole effluent sample is prepared and each dilution is individually combined with a culture of particle feeding flagellate to determine a dose response curve.

9. The method of claim 8, wherein the particle-feeding flagellate is *Teramitus rostratus* in flagellate form.

10. The method of claim 7, wherein the particle-feeding flagellate is *Teramitus rostratus* in flagellate form.

11. The method of claim 7, further comprising the steps of

recovering a particulate fraction from an aliquot of the whole effluent sample;

combining the particulate fraction with a third culture of particle-feeding flagellate;

determining the growth rate of the particle-feeding flagellate culture in the presence of the particulate fraction; and

comparing the growth rate of the particle-feeding flagellate culture in the presence of the particulate fraction to the growth rate in the presence of the unfiltered whole effluent sample.

12. The method according to claim 11, wherein a series of dilutions of the particulate fraction is prepared and each dilution is individually combined with a culture of particle feeding flagellate to determine a dose response curve.

13. The method of claim 12, wherein the particle-feeding flagellate is *Teramitus rostratus* in flagellate form.

14. The method of claim 11, wherein the particle-feeding flagellate is *Teramitus rostratus* in flagellate form.

15. The method of claim 1, further comprising the step of monitoring the growth of a second culture of particle-feeding flagellate in the presence of the whole effluent and comparing the growth of the first and second cultures, wherein the mean size of the flagellates in the first and second cultures is different.